## REMARKS

According to the Office Action of November 13, 2008, claims 16, 20-26, and 31-39 were examined and have been rejected under 35 U.S.C. § 112, first paragraph, and 35 U.S.C. § 103. In response, Applicants have amended claims 16 and 20, have canceled claims 21-24 and have added new claims 40 and 41. Thus, claims 16, 20, 25-26 and 31-41 are now pending.

Claims 16 and 20 have been amended to incorporate limitations previously presented in claims 24 and 21 respectively. Claim 16 was further amended to recite a method for the "reduction of risk" of an immune system-related disorder. This additional recitation is supported by the specification in passim (for example, at page 3, lines 19-25). Thus, no new matter has been added by these amendments.

In view of the amendments to the claims and remarks below, Applicants respectfully request that the rejections be reconsidered and withdrawn.

## REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH, ENABLEMENT

Claims 16, 20-26 and 31-39 have been rejected under 35 U.S.C. § 112, first paragraph. This rejection is moot with regard to claims 21-24 because these claims have been cancelled.

### I. THE SPECIFICATION ENABLES ONE TO PREVENT AN IMMUNE SYSTEM-RELATED DISORDER.

On page 2, the Office Action acknowledges that the specification enables one skilled in the art to make and use a treatment of immune system-related disorders, but that the specification does not enable one of ordinary skill in the art to prevent immune system-related disorders.

When asserting an enablement rejection, a reasonable explanation as to why the claims are not enabled by the specification must be set forth. *In re Wright*, 999 F.2d 1557, 1561-1562 (Fed. Cir. 1993); *In re Stoughton*, No. 2005-2235, App. No. 09/038,894, 2006 WL 1665412 at *4 (BPAI 2006). Precise predictability is not the standard to employ. *In re Corpet*, No. 2004-1790, App. No. 09/836,971, 2004 WL 2733634 (BPAI 2004).

In *Corpet*, the examiner rejected claim 12 as not enabled by the specification. 2004 WL 2733634 at *1. Claim 12 recited "[a] method of preventing colon or rectum cancer comprising administering to a mammal a therapeutically effective amount of a non-fermented osmotic polyol laxative." *Id.* The rationale for rejecting claim 12 was based on the argument

> that the recitation of preventing "extend[s] the treatment to those patients in which rectal and colon cancers may occur at any point of time in [the] future." [Citation omitted.] With respect to the state of the art, the examiner apparently recognizes that "[t]he state of the art recognizes that increased intake of dietary fibers contribute to the increased bowel movements and thus result in lowering the risk of colon cancers," but asserts that "the art does not teach or recognize a complete prevention of the above claimed cancers." [Citation omitted.] Finally, with respect to guidance of the specification and examples, the examiner focuses on the lack of teaching of an understanding of when the cancer may occur.

*Id.* at *1. The Board determined that the examiner's rationale required "precise predictability as to the time when the colon or rectal cancer will appear, and also appears to require 100% prevention. That is not, however, a requirement under 35 U.S.C. § 112, first paragraph." *Id.* at *2. Due to this flawed rationale, the Board held that the examiner failed to meet his burden and reversed the rejection. *Id.* at *3.

The Board reversed a similar rejection in *In re Goldenberg*, App. No. 08/183,381, 2002 WL 31105508 (BPAI 2002). In *Goldenberg*, the examiner argued that "'[a]pplicant broadly claims an anti-idiotype vaccine to prevent cancer, AIDS and malaria, but the specification fails to enable the vaccine(s) and effectively teach how to make and/or use said vaccines to achieve this.'" *Id.* at *3. The Board held that this

> failed to provide the evidence necessary to demonstrate that appellants' disclosure does not enable their claimed invention. While some of the claimed combinations may be inoperative, the examiner failed to establish that the number of inoperative combinations is so significant, that one of ordinary skill in the art would have to experiment unduly in order to practice the claimed invention.

*Id.* at *4. Like *Corpet*, the Board in *Goldenberg* reversed the rejection because the examiner required 100% predictability, which is not the standard for enablement.

As evident from these cases, there is no *per se* bar against claims directed to preventing a condition. Thus, there must be some evidence proffered that preventing the recited allergies is unpredictable. A non-enablement argument cannot be supported without citing some evidence. Like the rejections in *Corpet* and *Goldenberg*, this rejection does not offer the required evidence.

Moreover, like *Corpet*, there is sufficient evidence for one of ordinary skill in the art to conclude that the recited invention prevents cancer. In *Corpet*, the examiner recognized that "state of the art recognizes that increased intake of dietary fibers contributes to the increased bowel movements and thus result in lowering the risk of colon cancers." *Id.* at *1. Likewise, in this case, the specification admittedly enables the treatment of allergies. This, in turn, is recognized within the art as a means of lowering the risk and preventing the recited allergies.

On page 4, the Office Action contends that the Applicants have not provided a description of how allergies can be prevented. However, the Applicants have stated that the invention prevents allergies by maintaining or restoring the Th1/Th2 balance (specification at page 4, lines 1-3). Therefore, Applicants have provided, at least in theory (which Applicants do not intend to be bound by), a description of how allergies can be prevented.

On page 5, the Office Action contends that the specification does not provide working examples sufficient to support the prevention of the recited allergies. However, page 28 of the specification provides that

> administration of a combination of 1 wt. % GT and 1 wt. % AcOl resulted in a decrease in the Th2-related cytokines IL-4, IL-5 and IL-10, while the Th1-related cytokines IL-2 and IFN-γ were not lowered .... These results are indicative for the Th1/Th2 balancing effect of a combination of acid- and neutral oligosaccharides and indicative for the advantageous use of acid oligosaccharides in the present method, e.g. for the treatment and/or prevention of diseases with relatively low Th1 immunity. Particularly the IL-4/IFN ratio reflects the Th2/Th1 balance. In other words, a lower ratio is indicative for stimulation of Th1 and/or inhibition of Th2, and in any case indicative for the Th1-Th2 balancing effect of the present oligosaccharides.

As stated above, restoring and/or maintaining the Th1/Th2 balance prevents the recited allergies. Therefore, the specification provides an example that one skilled in the art would recognize as preventing the recited allergies.

Additionally, the clinical trials establish that the recited method prevents allergies. The clinical trial did not involve any measures, steps or features not described or derived from the present application. (See "Prevention of early atopic dermatitis by an infant formula supplemented with immunoactive prebiotics in low atopy risk infants," Abstract for the 27th EAACI Congress, June 7-11, 2008.)

**1. Response to Office Action of November 13, 2008**

On pages 9-11, the Examiner expresses doubt that the prevention of allergies is enabled by the specification. This doubt is contrary to the statement in the reference cited above – "This trial indicates a preventive effect of specific immunactive OS-supplemented formula feeding on the incidence of early [atopic dermatitis] in infants" – and is not supported by evidence. Assuming that the Examiner has established a lack of enablement (which the Applicants expressly deny), it is incumbent upon the Applicants "to present persuasive arguments, supported by suitable proofs where necessary, that one skilled in the art would be able to make and use the claimed invention using the disclosure as a guide." *Ex parte Cocito*, App. No. 08/975,338, 1999 WL 33287725 at *2(BPAI 1999). "In making the determination of enablement, the examiner shall consider the original disclosure and all evidence in the record, weighing evidence that supports enablement against evidence that the specification is not enabling." *Id.* In this case, there is no evidence that disputes the statements made in the abstract for the 27th EAACI Congress. Accordingly, when weighing the evidence, the only conclusion that can be reached is that the specification enables one to prevent the recited immune related disorders.

For these reasons, the specification provides guidance to make and use the recited invention without undue experimentation. Accordingly, Applicants respectfully request reconsideration and withdrawal of this rejection.

**REJECTION UNDER 35 U.S.C. § 103**

Claims 16, 20-26 and 31-39 have been rejected under 35 U.S.C. § 103 as being unpatentable over Ikemizu[1] in combination with Okada[2]. This rejection is moot with regard to claims 21-24 because these claims have been cancelled.

[1] JP 2003-221339 to Ikemizu *et al.* ("Ikemizu").
[2] EP 1 321 527 to Okada *et al.* ("Okada").

## I. RECITED INVENTION

In general, the invention relates to maintaining or restoring Th1/Th2 balance. The invention, as recited in amended claim 16, is directed to a method for the treatment, reduction of risk or prevention of an immune system-related disorder in a mammal. The immune system-related disorder is selected from the group consisting of allergy Type 1, allergy Type 2, allergy Type 3, and allergy Type 4. The method comprises administering to the mammal a composition comprising a therapeutically effective amount of an acid oligosaccharide and two chemically distinct neutral oligosaccharides. The acid oligosaccharide has a degree of polymerization between 1 and 250 and is prepared from pectin or alginate. The two chemically distinct neutral oligosaccharides comprising fructooligosaccharides and a second oligosaccharide selected from the group consisting of transgalactooligosaccharides, galactooligosaccharides and mixtures thereof.

## II. DIFFERENCES BETWEEN THE CITED REFERENCES AND THE CLAIMED INVENTION

Ikemizu discloses acid xylooligosaccharide,[3] which is not the recited acid oligosaccharide. Ikemizu's xylooligosaccharide has a xylose backbone where a uronic acid residue is attached as a side chain.[4] Xylooligosaccharides are made from xylose units. The uronic acid side chains disclosed in Ikemizu are glucuronic acid or 4-O-methyl-glucuronic acid; and therefore derived from glucose, not galactose, mannose or gulose.[5]

In contrast, the recited invention requires that the acid oligosaccharide be prepared from pectin or alginate. Pectin is a linear chain of α-(1-4)-linked D-galacturonic acid units. Within this backbone, D-galacturonic acid units are occasionally replaced with L-rhamnose units. Neutral sugars, such as xylose, may branch from these L-rhamnose units. Thus, while pectin may contain xylose, it is not a xylooligosaccharide as disclosed in Ikemizu.

Likewise, alginates are not xylooligosaccharides. Alginates are linear unbranched polymers containing β-(1-4)-linked D-mannuronic acid and α-(1-4)-linked

[3] Ikemizu at abstract.
[4] Ikemizu at translated page 3.
[5] Ikemizu at translated page 3.

guluronic acid residues.[6] It does not contain xylose; and therefore, it is not a xylooligosaccharide.

Neither pectin nor alginate would produce a xylooligosaccharide, nor would they have a uronic acid side chain. Only pectin comprises xylose, but xylose is not the backbone. Instead, it is a sugar residue that branches from the D-galacturonic acid backbone. Consequently, an acid oligosaccharide prepared from pectin or alginate could not have a xylose backbone with uronic acid side chains. Thus, in addition to the fact that Ikemizu does not teach administering a compound to treat immune system-related disorders, or the use of neutral oligosaccharides,[7] it additionally does not teach the recited acid oligosaccharide.

Additionally, uronic acid units themselves are different. Ikemizu discloses that the uronic acids residues are glucuronic acid or 4-O-methyl-glucuronic acids.[8] Therefore, the acid residues are derived from glucose. In contrast, alginate contains mannuronic acid and guluronic acid residues; and pectin contains galacturonic acid units. Therefore, the uronic acid units in pectin and alginate are derived from galactose, mannose and guluose. Consequently, these uronic acid units disclosed in Ikemizu are different from those in pectin or alginate.

According to the Office Action, Okada, teaches that atopic dermatitis can be treated with raffinose, an α-galactosyl oligosaccharide or netrual oligosaccharide.[9] However, Okada does not teach or suggest that xylooligosaccharides or acid oligosaccharide prepared from pectin or alginate can be used instead of an α-galactosyl oligosaccharide. Nor does Okada teach or suggest using two chemically distinct neutral oligosaccharides comprising fructooligosaccharides and a second oligosaccharide selected from the group consisting of transgalactooligosaccharides, galactooligosaccharides and mixtures thereof.

## III. ARGUMENT

When making a rejection under 35 U.S.C. § 103, the Examiner has the burden of establishing a *prima facie* case of obviousness. *In re Fritch*, 23 U.S.P.Q.2d 1780, 1783 (Fed. Cir. 1992). To establish this, each and every claimed element must be taught or made

[6] Specification at page 13, lines 11-12.
[7] Office Action at page 8.
[8] Ikemizu at translated page 3.
[9] Office Action at page 8.

obvious by the applied references. *Ex parte Hellums*, App. No. 09/103,704, 2003 WL 25281923 at *4 (BPAI Jul. 15, 2003); *Ex parte Likins*, App. No. 10/010,392, Appeal No. 2004-0760, 2004 WL 4981756 at *3 (BPAI Apr. 8, 2004).

As discussed above, the references do not teach an acid oligosaccharide prepared from pectin or alginate. Furthermore, the references do not teach using two chemically distinct neutral oligosaccharides comprising fructooligosaccharides and a second oligosaccharide selected from the group consisting of transgalactooligosaccharides, galactooligosaccharides and mixtures thereof.

The Patent Office must further establish some reason to combine the references. *KSR Int'l Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1731 (2007); *Takeda Chemical Industries, Ltd. v. Alpharpharm Pty., Ltd.*, 492 F.3d 1350, 1356-1357 (Fed. Cir. 2007). The *KSR Int'l* Court acknowledged the importance of identifying a reason that would have prompted a person of ordinary skill in the art to combine the elements in the way the claimed invention does. *KSR Int'l*, 127 S.Ct. at 1731; *Takeda Chemical*, 492 F.3d at 1356-1357. Repeatedly throughout the *KSR Int'l* decision, the Court discussed the importance that the result obtained by a particular combination was predictable to one of ordinary skill in the art. *KSR Int'l*, 127 S.Ct. at 1731 and 1739-1742.

Here, there is no reason to substitute Ikemizu's xylooligosaccharides with the recited acid oligosaccharides. One of ordinary skill in the art would not reasonably believe that oligosaccharides having different structures are equivalent or can be substituted for one another. Instead, one would expect different oligosaccharides to have completely different effects. Therefore, one would not have a reason to replace one oligosaccharide, such as Ikemizu's xylooligosaccharide, with another, such as the recited acid oligosaccharides prepared from pectin or alginate, because one would not reasonably expect the effects to be the same. Furthermore, there is no reason to substitute Okada's neutral oligosaccharides with those recited in claim 16.

## CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully submit that all pending claims in the instant application are patentable over the prior art and

are in condition for allowance. Accordingly, reconsideration and withdrawal of the asserted rejections and a Notice of Allowance are respectfully requested.

Should the Examiner have any questions or concerns, the Examiner is invited to contact the Applicants' undersigned attorney by telephone at 412-471-8815.

Respectfully submitted,

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